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GP 1646

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 98-385-J)

In re Application of: Hauptmann et al.	
Serial No.: 09/899,429	**Before the Examiner: E. O'Hara**
Filed: July 3, 2001	**Group Art Unit: 1646**
For: TNF Receptors, TNF Binding Proteins and DNAs Coding For Them	

Commissioner for Patents
Washington, D.C. 20231

Sir:

TRANSMITTAL LETTER

1. We are transmitting herewith the attached papers for the above-described patent application: Response to Office Action and return postcard.

2. GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES: Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2490.

3. CERTIFICATE OF MAILING BY "EXPRESS MAIL" UNDER 37 C.F.R. 1.10: The undersigned hereby certifies that this Transmittal Letter and the papers, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as "Express Mail Post Office to Addressee" in an envelope addressed to: Commissioner for Patents, Washington D.C. 20231, on October 15, 2002.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: October 15, 2002

By: _____
Donald Zuhn, Ph.D.
Reg. No. 48,710

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 98-385-J)

PATENT

In re Application of: Hauptmann et al.

Serial No.: 09/899,429

Filed: July 3, 2001

For: TNF Receptors, TNF Binding Proteins and DNAs Coding For Them

Before the Examiner: E. O'Hara

Group Art Unit: 1646

#13
10/28/02

Commissioner for Patents
Washington, D.C. 20231

Sir:

RESPONSE TO RESTRICTION REQUIREMENT MAILED SEPTEMBER 12, 2002

Responsive to the Restriction Requirement, mailed September 12, 2002, Applicants elect to prosecute those claims directed to methods for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a TNF binding polypeptide of SEQ ID NO: 4 or SEQ ID NO: 6, designated as Group I by the Examiner, with traverse. The basis for Applicants' traversal of the requirement is as follows.

Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to methods for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a TNF binding polypeptide of SEQ ID NOs: 2, 4, 6, 8, 12, 14, 16, 18, or 20. A ClustalW multiple sequence alignment of these polypeptides is shown in Exhibit A. The sequence alignment was performed using the application MacVector 7.1.1 (Accelrys, Cambridge, UK; http://www.accelrys.com) at the default settings. This sequence alignment indicates that there is a substantial degree of homology between the amino acid sequences set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20.

The amino acid sequence of the TNF receptor protein is set forth in SEQ ID NO: 2 (specification p. 5, ln. 7-39). The amino acid sequence consisting of residues 41 to 201 of SEQ ID

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NO: 2 (which is equivalent to the amino acid sequence set forth in SEQ ID NO: 4) encodes a secretable TNF-binding protein (specification p. 4, ln. 27-41). As shown in Exhibit A, the polypeptides set forth in 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 all possess this portion of the TNF receptor protein. Moreover, this portion constitutes between 76.3% (SEQ ID NO: 8) and 99.4% (SEQ ID NO: 6) of the polypeptides set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20. With the exception of an addition of methionine residue at the 5' end of the polypeptides set forth in SEQ ID NOs: 6, 10, 16, and 20, the polypeptides set forth in SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 differ only by the presence or absence of sequences encoding the signal peptide (amino acid residues 1 to 29 of SEQ ID NO: 2; specification p. 21, ln. 35 to p. 22, ln. 1), the portion of pro-protein cleaved following secretion (amino acid residues 30 to 40 of SEQ ID NO: 2; specification p. 22, ln. 7-11), and the linker region (amino acid residues 202 to 211 of SEQ ID NO: 2; specification p. 22, ln. 12-15) of the TNF receptor protein. Applicants respectfully submit that there will be no undue hardship on the Office in performing a search with respect to methods for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a TNF binding polypeptide of SEQ ID NOs: 2, 4, 6, 8, 12, 14, 16, 18, or 20, since a search for methods for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a TNF binding polypeptide of SEQ ID NO: 4 or SEQ ID NO: 6 will identify all of the non-elected sequences.

Applicants do not believe any additional fee is required. However, the Commissioner is authorized to charge any deficiency to Deposit Account No. 13-2490. If Examiner O'Hara believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: October 15, 2002

By: _____
Donald Zuhn, Ph.D.
Reg. No. 48,710

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EXHIBIT A

ClustalW (v1.4) multiple sequence alignment

10 Sequences Aligned Alignment Score = 54899
Gaps Inserted = 2 Conserved Identities = 161

Pairwise Alignment Mode: Slow
Pairwise Alignment Parameters:
    Open Gap Penalty = 10.0 Extend Gap Penalty = 0.1
    Similarity Matrix: blosum

Multiple Alignment Parameters:
    Open Gap Penalty = 10.0 Extend Gap Penalty = 0.0
    Delay Divergent = 40% Gap Distance = 8
    Similarity Matrix: blosum

Processing time: 3.5 seconds

```
SEQ 2     1 MGLSTVPDLLLPLVLLELLVGIYPSGVIGLVPHLGDREKRDSVCPQGKYI  50
SEQ 4     1                                        DSVCPQGKYI  10
SEQ 6     1                                       MDSVCPQGKYI  11
SEQ 8     1 MGLSTVPDLLLPLVLLELLVGIYPSGVIGLVPHLGDREKRDSVCPQGKYI  50
SEQ 10    1                              MLVPHLGDREKRDSVCPQGKYI  22
SEQ 12    1 MGLSTVPDLLLPLVLLELLVGIYPSGVIG----------DSVCPQGKYI  39
SEQ 14    1 MGLSTVPDLLLPLVLLELLVGIYPSGVIGLVPHLGDREKRDSVCPQGKYI  50
SEQ 16    1                              MLVPHLGDREKRDSVCPQGKYI  22
SEQ 18    1 MGLSTVPDLLLPLVLLELLVGIYPSGVIG----------DSVCPQGKYI  39
SEQ 20    1                                       MDSVCPQGKYI  11
                                                   **********

SEQ 2    51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL 100
SEQ 4    11 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  60
SEQ 6    12 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  61
SEQ 8    51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL 100
SEQ 10   23 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  72
SEQ 12   40 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  89
SEQ 14   51 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL 100
SEQ 16   23 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  72
SEQ 18   40 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  89
SEQ 20   12 HPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCL  61
            **************************************************

SEQ 2   101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 150
SEQ 4    61 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 110
SEQ 6    62 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 111
SEQ 8   101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 150
SEQ 10   73 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 122
SEQ 12   90 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 139
SEQ 14  101 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 150
SEQ 16   73 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 122
SEQ 18   90 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 139
SEQ 20   62 SCSKCRKEMGQVEISSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCL 111
            **************************************************
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SEQ 2    151 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 200
SEQ 4    111 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 160
SEQ 6    112 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 161
SEQ 8    151 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 200
SEQ 10   123 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 172
SEQ 12   140 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 189
SEQ 14   151 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 200
SEQ 16   123 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 172
SEQ 18   140 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 189
SEQ 20   112 NGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIE 161
             **************************************************

SEQ 2    201 NVKGTEDSGTTVLLPLVIFFGLCLLSLLFIGLMYRYQRWKSKLYSIVCGK 250
SEQ 4    161 N                                                  161
SEQ 6    162 N                                                  162
SEQ 8    201 NVKGTEDSGTT                                        211
SEQ 10   173 NVKGTEDSGTT                                        183
SEQ 12   190 NVKGTEDSGTT                                        200
SEQ 14   201 N                                                  201
SEQ 16   173 N                                                  173
SEQ 18   190 N                                                  190
SEQ 20   162 NVKGTEDSGTT                                        172
             *

SEQ 2    251 STPEKEGELEGTTTKPLAPNPSFSPTPGFTPTLGFSPVPSSTFTSSSTYT 300
SEQ 4    162                                                    161
SEQ 6    163                                                    162
SEQ 8    212                                                    211
SEQ 10   184                                                    183
SEQ 12   201                                                    200
SEQ 14   202                                                    201
SEQ 16   174                                                    173
SEQ 18   191                                                    190
SEQ 20   173                                                    172

SEQ 2    301 PGDCPNFAAPRREVAPPYQGADPILATALASDPIPNPLQKWEDSAHKPQS 350
SEQ 4    162                                                    161
SEQ 6    163                                                    162
SEQ 8    212                                                    211
SEQ 10   184                                                    183
SEQ 12   201                                                    200
SEQ 14   202                                                    201
SEQ 16   174                                                    173
SEQ 18   191                                                    190
SEQ 20   173                                                    172
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```
SEQ 2    351 LDTDDPATLYAVVENVPPLRWKEFVRRLGLSDHEIDRLELQNGRCLREAQ 400
SEQ 4    162                                                    161
SEQ 6    163                                                    162
SEQ 8    212                                                    211
SEQ 10   184                                                    183
SEQ 12   201                                                    200
SEQ 14   202                                                    201
SEQ 16   174                                                    173
SEQ 18   191                                                    190
SEQ 20   173                                                    172

SEQ 2    401 YSMLATWRRRTPRREATLELLGRVLRDMDLLGCLEDIEEALCGPAALPPA 450
SEQ 4    162                                                    161
SEQ 6    163                                                    162
SEQ 8    212                                                    211
SEQ 10   184                                                    183
SEQ 12   201                                                    200
SEQ 14   202                                                    201
SEQ 16   174                                                    173
SEQ 18   191                                                    190
SEQ 20   173                                                    172

SEQ 2    451 PSLLR 455
SEQ 4    162       161
SEQ 6    163       162
SEQ 8    212       211
SEQ 10   184       183
SEQ 12   201       200
SEQ 14   202       201
SEQ 16   174       173
SEQ 18   191       190
SEQ 20   173       172
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